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13. ABSTRACT ***(Maximum 200 Words)***

Since the overall risks and benefits of hormonal replacement therapy (HRT) in breast cancer survivors are not clearly established, and it is unlikely that a definitive answer will be available in the near future, we developed a decision analytic computer model for individualizing decisions, using the best available literature estimates for all currently known or suspected benefits and adverse outcomes. In addition, the model allows input of individual risk factors for breast cancer recurrence, coronary artery disease, osteoporosis, etc., and allows weighting of patients' preferences for these outcomes. We found that women at average risk for coronary heart disease (CHD) and hip fracture lose 4.3 quality-adjusted life months (QALMs) by taking HRT. Women who value the CHD and hip fracture states as having the worst impact on health and breast cancer recurrence as having the mildest impact on health lose the least from HRT, 3.6 QALMs. Women who value the CHD and hip fracture states as having the mildest impact and breast cancer recurrence as having the worst impact on health lose 5.3 QALMS. Therefore, unless future studies show a larger benefit on CHD mortality or other health states, HRT decisions for breast cancer survivors should include careful consideration of individual preferences for all of the potential outcomes. The model can readily incorporate data on new treatments and other outcomes as they become available.

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BODY

INTRODUCTION

This is a revised final report. A one-year extension was requested for further data analysis, which is still ongoing. We hope to submit a paper soon. Also, due to an editing error in our office, not all the pages intended were submitted. We apologize and have included the full document, which we hope is now satisfactory.

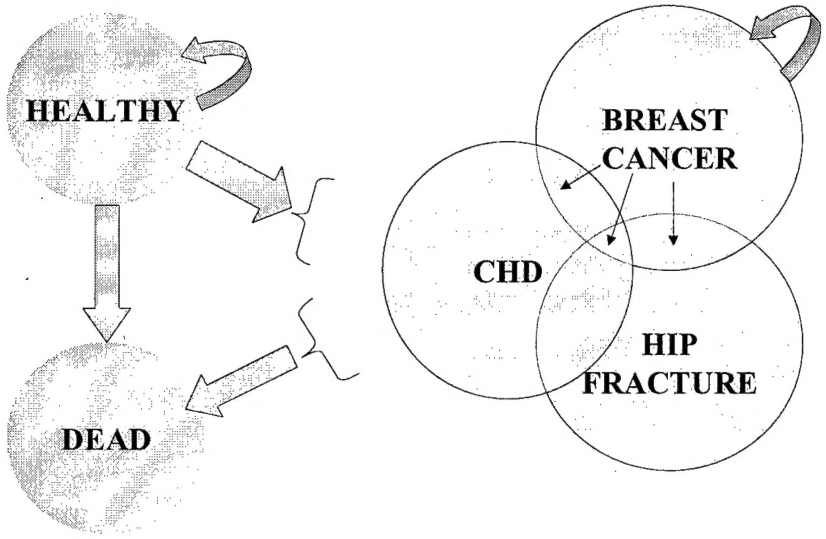
Unfortunately, during the course of this project, additional data were published casting doubt on the usefulness of HRT for reducing or preventing coronary disease, making the development of a shared decision making computer package pointless. Contrary to our original hypothesis, there is now really no reason for a breast cancer survivor to consider HRT for prevention of CAD (technical objectives 5 and 6)

METHODS

A decision analysis was performed for 60-year old women breast cancer survivors who are considering hormone replacement therapy (HRT) as preventive medicine for coronary heart disease (CHD) and osteoporosis. The outcome measure was quality-adjusted life months (QALMs) life expectancy with each option. A base case analysis was performed for women at average risk for CHD and osteoporosis. A sensitivity analysis was performed for women at higher or lower risks for each disease. HRT was assumed to be combined estrogen and progesterone for women with intact uteruses or estrogen alone for women who have had hysterectomies.

The decision analysis was performed with a Markov transition state model (DATA, TreeAge Software, Williamstown, MA). The model begins with two hypothetical cohorts of healthy women, one choosing HRT and one declining it. Each year some women develop CHD, hip fracture, breast cancer, or combinations of these diseases. Each year they also risk death from these diseases or from other general population causes related to their age, sex and race (Vital Statistics).

Markov Model



For simplicity, the transitions between the CHD and HIP fracture state and other states are not shown; they are the same as for the breast cancer state.

RESULTS

The assumptions used in the analysis for these risks and the effect of HRT on the risks are shown in table 1. Rates taken from the literature were transformed to probabilities for use in the model.

TABLE 1: ASSUMPTION

OUTCOME	RATE OR PROBABILITY	RELATIVE RISK	REFERENCE
Breast Cancer Recurrence	Cumulative Recurrence Yr 1, 11% Yr 5, 41.2% Yr 10, 56%	-------	Early Breast Cancer Trialists Collaborative Group
CHD Risk	Annual Probability 0.21% at age 50 yrs to 0.48% at age 60 yrs and greater	-------	Lloyd-Jones
Hip Fracture Incidence	Incidence, per 100,000 White women, 33.9 at age 50.1 yrs to 1731.5 at age 80 yrs Nonwhite women, 18.4 at age 50 yrs to 880.6 at age 80 yrs	-------	Farmer ME
Effect of HRT on Breast Cancer Risk	------	Any Use 1.27	Collab. Grp. On Hormonal Factors in Br. Cancer
Effect of HRT on Hip Fracture Risk	------	0.75	Grady D, et al
Effect of HRT on CAD Risk	------	Yr 1 1.52 (1.01-2.29) 2 0.98 (0.66-1.46) 3 0.85 (0.54-1.33) ≥4 0.75(0.50-1.13)	Herrington
Annual Risk of Dying after developing Breast Cancer	Disease specific mortality probability 0.0324		Early Breast Cancer Trialists Group
Ann Risk of Dying after developing CHD	9.6% in first yr 2.6% in subsequent yrs		Col
Ann Risk of Dying after Hip Fracture	17% in first yr		Col

Utilities (Table 2)

We conducted interviews on a convenience sample of 30 women from the breast cancer clinics at 2 tertiary care centers to assess their utilities. Using a computerized interview equipped with the U-titer II program (Sumner), women assigned a utility to each potential health state by means of the standard gamble technique. [We also measure utilities for some of the states using a visual analog scale]. Health state descriptions were developed for both acute and chronic scenarios for outcomes relevant to use of HRT. The acute states lasted 6 months and resolved completely with return to current health. For these states the women gambled the health state versus some probability of ideal health or 6 months of severe, constant pain, with the choices following a bisection of probabilities. The chronic health states were described as stable conditions that last for the remainder of the woman's life expectancy, which was calculated from a simple life table. These states were developed using an adaptation of Torrance's Health Utility Index II and included 8 key dimensions. For these states the women gambled the health state versus some probability of ideal health or death, again with the choices following a bisection of probabilities. The utilities for each state are shown in Table 2.

Table 2 Utilities of chronic health states

Health States Median (Interquartile Range)	**Overall N=81**	**Breast Clinic N=30**	**GIM Clinic N=51**
Current Health	.99 (.93-1)	.98 (.93-1)	1 (.92-1)
KEY CHRONIC STATES			
Stage I breast cancer	.98 (.91-1)	.99 (.93-1)	.97 (.90-1)
Cyclic HRT	1 (.95-1)	.99 (.95-1)	1 (.93-1)
Chronic angina (class III)	.90 (.59-.98)	.91 (.75-.97)	.90 (.5-.99)
Post hip fracture, poor result	.84 (.50-.93) *	.89 (.75-.93)	.75 (.02-.93)
Constant Pain (6 mo.)	.93 (.61-1)	.96 (.75-.99)	.93 (.59-1)
OTHER CHRONIC STATES			
Metastatic Breast Cancer	0 (0-.50) N=19	0 (0-.50) N=11	.06 (0-.37) N=8
Post Vertebral Fracture	.97 (.86-.98) N=21	.98 (.93-.98) N=10	.86 (.74-.99) N=11
Chronic menopausal problems	.99 (.93-1) N=16	1 (.99-1) N=6	.96 (.93-1) N=10
Alzheimer's Disease	.24 (0-.5) N=18	.49 (0-.75) N=3	0 (0-.5) N=15
Chronic Post CVA	.61 (.26-.75) N=13	.5 (.41-.74) N=3	.68 (.24-.96) N=10

* $p<.05$ for Wilcoxon Rank Sum comparison between 2 groups.

Table 3. Utilities of acute health states

Health States Median (Interquartile Range)	**Overall** *	**Breast Clinic**	**GIM Clinic**
KEY ACUTE STATES			
Acute MI	.97 (.89-1) N=25	.97 (.89-1) N=11	.97 (.83-1) N=14
Acute Hip Fracture	.99 (.90-1) N=23	1 (.93-1) N=6	.98 (.90-1) N=17
New Breast Cancer	1 (.85-1) N=19	.99 (.87-1) N=7	1 (.77-1) N=12
Acute Menopausal Symptoms	1 (1-1) N=14	1 (1-1) N=6	1 (.96-1) N=8
Health States Median (Interquartile Range)	**Overall** *	**Breast Clinic**	**GIM Clinic**
OTHER ACUTE STATES			
Vaginal Bleeding	1 (1-1) N=10	1 (1-1) N=2	1 (1-1) N=8
Acute DVT	1 (.71-1) N=10	1 (1-1) N=4	.74 (.33-1) N=6
Acute PE	.99 (.79-1) N=11	.99 (.97-.99) N=5	.90 (.49-1) N=6
New Colon Cancer	1 (.99-1) N=8	1 (1-1) N=3	1 (.98-1) N=5
Acute CVA	.98 (.95-1) N=13	.99 (.95-1) N=7	.97 (.59-1) N=6
Acute Cholecystitis	1 (1-1) N=11	1 (.98-1) N=4	1 (1-1) N=7

* Utilities were not significantly different between the 2 groups.

Table 4

Demographic Characteristic	**Overall** N=81	**Breast Clinic** N=30	**GIM Clinic** N=51	**p** *
Mean Age (SD)	61	61	61	.98
Race (%)				.02
African American	29	10	41	
White	83	54	65	
Other	7	4	5	
Education (%)				.003
High school	36	13	50	
Some college or college	35	43	30	
Some graduate school	29	43	20	
Household Income (%)				.004
< $20,000	14	7	19	
$ 20- 59,999	43	26	53	
> 60,000	43	67	28	
Married (%)	56	77	44	.004

* p-value for Chi^2 except as noted

† p-value for t-test

Characteristic	Overall N=81	Breast Clinic N=30	GIM Clinic N=51	p
Past Medical History (%)				
Breast Cancer	39	100	0	<.001
Coronary Heart Disease	16	16	16	.96
Osteoporosis	11	16	8	.24
Medications (%)				
HRT Current	29	0	47	
HRT Past	32	55	18	<.001
Tamoxifen Ever	19	51	0	<.001
Oral contraceptives ever	40	45	37	.48
Family History (%)				
Breast Cancer	28	26	29	.72
Coronary Heart Disease	60	58	61	.81
Osteoporosis	18	32	12	.02

DISCUSSION

- Estimated benefits from HRT vary with
  - Risk status
  - Race
  - Age
  - Utilities assigned to health states

- The largest difference comes from choice of source of estimate for benefit on CAD- currently there are no clear answers. Women and their physicians must choose between

  1) a large amount of observational data which suggests a large benefit
  2) a small amount of RCT data (on a different question - 2° prevention) which shows a small benefit

- For BCS, the only conditions that result in gains in quality-adjusted life expectancy are combinations of the most optimistic assumptions regarding quality of life with breast cancer and the effect of HRT on the risk of breast cancer recurrence and the most pessimistic assumptions regarding quality of life with CHD and hip fracture and the effect of HRT on the risk of CHD and hip fracture.

Limitations

- Not all outcomes potentially affected by HRT are included in the model. (e.g.: Alzheimer's disease, colon cancer, stroke)

- Not all possible interventions are included in the model. (e.g.: raloxifene, alendronate, statins)

KEY RESEARCH ACCOMPLISHMENTS

- Women at average risk for CHD and hip fracture lose 4.3 QALMS by taking HRT.
- Women who value the CHD and hip fracture states as having the worst impact on health and the breast cancer state as having the mildest impact on health lose the least from HRT, 3.6 QALMS.
- Women who value the CHD and hip fracture states as having the mildest impact on health and the breast cancer state as having the worst impact on health lose 5.3 QALMS.
- Depending on the utility values chosen for health states and on individuals' risk factors for disease, HRT results in a loss of 0.2 QALMS (for women with a high risk for CHD and hip fracture) or a loss of 6.1 QALMs (for women with a low risk for CHD and hip fracture).
- Our base case analysis used the HRT effect on CHD risk found in the HERS trial, an increased risk in the first year, then a decrease in risk by year 3. In a sensitivity analysis, we calculated outcomes using the HRT effect on CHD risk found in observational studies, a relative risk of 0.51. The benefits of HRT are somewhat greater under these conditions. Depending on the utility values chosen for health states and on individuals' risk factors for disease, HRT results in gains in quality-adjusted life expectancy as great as 3.3 QALMs or losses as great as 5.4 QALMs.

REPORTABLE OUTCOMES

Our results were presented at the Society for General Internal Medicine national meeting in Boston, MA, May, 2000, and at the DOD Era of Hope meeting in Atlanta, GA, June, 2000.

CONCLUSIONS

Unless future studies show a larger benefit on CHD mortality or other health states, HRT decisions for BCS should include careful consideration of individual preferences for all of the potential outcomes. The model can readily incorporate data on new treatments and other outcomes as they become available.

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